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The Bristol Medico-Chirurgical Journal

" Scire est nescire, nisi id me
Scire alius sciret.

JULY, 1923.

THE LONG FOX LECTURE:

DELIVERED IN THE UNIVERSITY OF BRISTOL ON MARCH 27TH, 1923.

T. LOVEDAY, M.A., *Vice-Chancellor, in the Chair.*

BY

PROFESSOR F. FRANCIS, D.Sc.,

Pro-Vice-Chancellor and Professor of Chemistry in the University of Bristol.

ON

THE RELATION BETWEEN CHEMISTRY AND MEDICINE.

THE practice of Medicine—in so far as it is strictly scientific—is based on the principles established by Physiology, Pathology and Pharmacology, and the history of these shows that they have progressed as their generalisations came to be based upon the experimental results of Biology, Chemistry and Physics.

The great and complex problems of Biology which lie at the foundations of Physiology and Pathology are being

resolved slowly into factors studied with the aid of the Atomic Theory and the Laws of Energy.

It seems to me, indeed, as though all other lines of research and avenues of progress in Medicine during the past fifty years have become comparatively deserted for those where advances are made through the technique and theories of Chemistry.

This period has seen a forbidding and difficult field of chemical research explored by the great chemists and physicists of the times, and I propose to place before you the main lines of thought which have brought about a profound change in the scientific aspect of Medicine.

The beginning of the nineteenth century saw the establishment of the conception of the Indestructibility of Matter, experimentally tested by Landolt in 1893, and shown to be a statement of fact to a degree of accuracy of one in ten millions. The study of that part of matter called Chemical Compounds, characterised by the constancy of their composition, led Dalton in 1808 to resuscitate the old Greek doctrine of Atoms advocated by the school of Leucippus.

Gay-Lussac and Humboldt in 1805 had investigated the composition of Steam, and discovered the extremely simple laws of gaseous combination. Six years later Avogadro, and eight years later Ampère, had interpreted these laws by a modification of the Atomic Theory, the assumption of Atomic complexes—called Molecules—and the resulting confusion of thought was only cleared up by Cannizaro in 1858.

At a date when Dr. Long Fox must have been losing interest in Chemistry, owing to the pressure of purely medical work, the broad basis of the science as it is known to-day was established.

The study of Chemical Compounds, interpreted by means

of this wonderful conception of Atoms, dominated Chemistry to the exclusion of everything else for the remaining part of the century.

Another great landmark in Science, corresponding to the discovery of the conservation of Mass at the beginning of the century, was the realisation by Meyer in 1842 that energy, like matter, was indestructible. Known as the First Law of Thermodynamics, it was placed on a firm experimental basis by Joule in 1843.

This principle, however, gives no information as to the direction in which a given process takes place, and the solution of this aspect of the problem was made by Clausius and Lord Kelvin in 1850, who framed the Second Law of Thermodynamics. These laws, developed mathematically, formed a non-hypothetical system of reasoning called Thermodynamics, which dominates Physical and an ever-increasing part of Chemical and even Biological science.

Chemical and Physical phenomena can be interpreted by means of the Atomic and Molecular hypothesis, extended by the Kinetic Theory of Matter, but the results arrived at may be open to question, because the assumptions used in these theories may not be justified. But, on the other hand, there is this alternative method of Thermodynamics, against which no such criticism can be made. This method is independent of any conception of the constitution of matter, or of any physical picture one may like to adopt of the processes at work.

Down to the period—and to fix a date let me say the early sixties—Chemistry had the marvellous weapon of the Atomic Theory ready for the wonderful victories made during the remainder of the century, and a potential weapon, Thermodynamics, the use of which towards the end of the century introduced the conception of continuity and revolutionised the science.

I will trace, to begin with, the Atomic-Molecular Theory of Matter; and there is not sufficient time at my disposal to discuss those brilliant and fascinating discoveries of the last twenty years, which have completely altered our conception of the nature of the Atom.

For a century that word had meant to chemists the limit of matter. By a variety of completely independent methods physicists had counted the number of these Atoms in a given space; the agreement between the results was so striking—numerically varying but little from the errors involved in taking the census of any large city—that the belief arose that matter was really composed of Atoms, and that it was no longer necessary to look upon the conception as merely a useful working hypothesis.

Then came the discovery of Radiation, the realisation of the existence of an intra-atomic world; the Atom was no longer the limit of matter, and we can now state that "Nature uses the same standard bricks in the construction of the Atoms of all elements, and that these standard bricks are the primordial atoms of positive and negative electricity, Protons and Electrons."

The wonder, beauty and magic of these discoveries are so great that I hope a scientific Milton of the future will arise to describe them for the benefit of that great part of intellectual mankind which is ignorant of Science. This work forms the most majestic monument to the human intelligence that the world has yet seen.

The outcome of the application of the Molecular Theory to Chemical compounds was the very simple conception of Valency, that the atoms were capable of holding together a definite number of other atoms. Hydrogen being taken as unit, Oxygen could combine with two of these atoms, Nitrogen with three, Carbon with four; this enabled pictures to be drawn of the architecture of the Molecule,

and upon this conception rose the edifice of Organic Chemistry.

This branch of the science commenced with the study of the products of Animal and Vegetable Metabolism. It had been freed from the incubus of Vital Force, supposed to be essential for their preparation, by the artificial production of Urea by Wöhler in 1828; but it was soon realised that the known methods were insufficient to cope with these highly complex substances, and their study was dropped for fifty years.

In the meanwhile Synthetic Organic Chemistry advanced, with the result that at present something like 100,000 new substances are known, their physical and chemical properties have been correlated with molecular architecture; a completely new technique has been invented, and a battery of weapons elaborated, which have enabled chemists during the past thirty years to take up again the study of those highly complex compounds, which play an all-important part in the activity of the living cell.

Throughout this period of some sixty to seventy years the conception of Valency has been the guiding star, offering an explanation—often uncanny—for all the curious phenomena met with. Its extension in 1874, by Le Bel and Van't Hoff, from two to three dimensions opened up new fields of thought, and a new chapter of Science was commenced, fraught with great importance to Medicine in the future.

Before I pass to those recent achievements so intimately connected with Biology let me remind you of some of the old victories. The molecular architecture of Alizarin was determined by Grebe and Leebermann in 1867; as a consequence it was synthesised in the following year, and before 1873—manufactured on a commercial scale—it had ousted the natural product from the markets of the world.

Between 1865 and 1882 Von Beyer, in Munich, had been engaged in investigating some of the most subtle problems in Organic Chemistry, and in the course of his work synthesised Indigo Blue and determined the arrangements of the atoms in the very complex molecule of this substance. Before this material could become an article of commerce yields had to be increased, and new methods of preparing intermediate products had to be devised. Time, skill, and an appreciation of the value of Science resulted in Synthetic Indigo from the Rhine factories replacing the natural product from our possessions in the East.

Ladenburg in 1886 effected the complete synthesis of Conine, one of the alkaloids of Hemlock, identical in all respects with the natural product; it was the first of the many striking feats of the extension of the conception of Valency to three dimensions.

From the study of Synthetic Organic Chemistry arose the industries of the dyes, perfumes, drugs and high explosives.

I have now come to that period—let us say the late eighties—when the accumulated experience of Synthetic Organic Chemistry had enabled chemists again to take up the study of those complex compounds so intimately connected with all life processes.

It was at this period, however, that a group of chemists with conceptions borrowed from Physics, were throwing a completely new light on chemical processes; but it will, I think, be more convenient if I follow the work of those distinguished organic chemists who achieved so much by the application of the old conceptions of molecular structure to the substances around which the phenomena of life are manifested.

I can continue this sketch because fortunately the discoveries of the current century have not yet seriously

disturbed the principles underlying systematic Organic Chemistry.

The problems facing the chemist who studies the products of animal and plant life are so extremely difficult and complex that it is only the master of his craft who can isolate here and there a specific problem among the multitude, and to that problem apply the knowledge of to-day.

The starches, fats and proteins of our food, all insoluble in water, are smoothly and rapidly rendered transmissible to the blood, and it is only up to a point that we can follow this progress by comparison with similar reactions, which can be carried out in the laboratory. But following such analyses, synthetic processes are at work, the mechanism of which we are in total ignorance. A true knowledge of metabolic processes can only be obtained by the tedious unravelling of the complex system of chemical changes into individual chemical reactions. We only know a very few of these simple reactions, but there is every hope in the future that we may be able to construct an accurately itemised account of the chemical transactions of the animal body—anabolic and katabolic. The value of such knowledge for the advancement of Medicine is obvious.

The day has long since passed when the statement that—fats and sugars are oxidised in the body to carbon dioxide and water and proteins give urea in addition—is considered to be an all-sufficient explanation of the chemical role of the substances in the animal economy.

The Enzymes produced in the cells have not been synthesised by the chemist, in fact the great majority have not yet been isolated in purified form. Willstätter, however, is publishing a series of papers on Enzymes from vegetable sources and most valuable results have been obtained.

The Proteins.—The proteins are among the most complex substances produced in the animal and plant world. They occupy a unique position in the activities of all living matter, and a complete comprehension of their nature must obviously precede the full development of Bio-chemistry. Even their isolation in a state of purity is difficult, and their present classification, certainly of physiological importance, is little more than a monument to our scientific ignorance of this extraordinarily important group of substances.

On hydrolysis they break down to relatively simple substances, the so-called Amino Acids, and as a result of the investigations of a century some twenty of these acids have been isolated, their molecular architecture determined, and their actual synthesis accomplished in the laboratory.

It is believed that all the various proteins are built up of some or many of these twenty acids, and it was to the genius of Emil Fischer that we owed the wonderful attempt to use these substances, and from them reconstitute the original protein material; it met with but partial success, and up to the present no synthesis of a protein has been effected. Not only has it been found impossible to effect a synthesis, but the actual analysis of the great majority of protein substances has defeated the chemist. We have been unable to devise a method of determining the total amount of the various Amino Acids, resulting from the degradation of the protein. We know that some are rich in one acid, others in another, and by feeding experiments on animals much valuable information has been obtained—enough to put the whole question of Protein assimilation in an entirely new light, and to show the incalculable advantage to Medicine of complete knowledge of this subject.

Upon a knowledge of the Proteins, constituting the major part of living protoplasm, depends in all probability a

knowledge of the Ferments or Enzymes, for it seems probable that proteins are the material from which the organism prepares these wonderful agents.

There is another aspect of the chemical study of the Amino Acids, which appears likely to prove of the highest importance to Medicine. Such Amino Acids as Phenylalanine, Tyrosine, Tryptophane and Histidine are always present in the intestines; they are the harmless breakdown products of the proteins, but when these are acted upon by certain micro-organisms, capable of breaking off carbon dioxide extremely toxic substances result. It has been suggested that this may be the right direction for the chemical investigation of alimentary toxæmia and its alleged consequences, such as arterio-sclerosis and chronic renal diseases. If such toxic bases are generated in sufficient amount and taken into the blood in quantity too large for transformation (by the liver and other defensive organs) into less harmful derivatives, they must inevitably manifest their pharmacological and toxic properties. One of these bases, probably formed from Histidine, is said to stimulate the isolated uterus to contraction in the almost unbelievable dilution of one in 250 millions.

Nucleic Acids.—The Nucleins and Nucleo-proteids are important constituents of cell nuclei, and some extremely interesting work has been carried out during the past forty years on Nucleic Acid, a constituent of the latter material.

May I remind you of the isolation in 1868 of Nucleic Acid from pus cells, followed in 1874, by the discovery that the spermatozoa heads of the Rhine salmon consist almost entirely of Protamine Nucleate, and that this must have arisen, not directly from food, but from muscle protein. These acids obtain the Carbohydrates and Phosphoric Acid required by their syntheses from the nourishment on which the organism thrives, but do not owe the purine factor to

the same source. In other words, the tissue must have the power to synthesise the purine nucleus, but we are still ignorant of the mechanism by which this synthesis is effected.

The transformations undergone by Nucleic Acid in contact with tissue extracts—that is, in the presence of Enzymes—have been studied for over thirty years, and we now have some idea of the smoothness and ease with which the living body converts Nucleic Acid into Uric Acid, and of the localisation and distribution of the Enzymes which bring about such changes.

I have no time to outline the investigations that have been carried out with such great success on the Pigments of Blossoms and Fruits, but I cannot refrain from drawing your attention to that on Chlorophyll and Hæmoglobin, which culminated in 1914.

It is to the genius of Willstätter that we owe the discovery of the chemical relationships between the two; for an assemblage of substituted Pyrrol nuclei constitute the basic architecture of the blood pigment and of Chlorophyll, iron playing the essential part in the former Magnesium a corresponding role in the latter.

I am going to say little on the question of Synthetic Drugs. When we consider the enormous number of substances synthesised during the past fifty years, numbering certainly something like 100,000, it is disappointing to have to record the few that have been found to possess pharmacological value, or certainly novel pharmacological reaction. A substance like Salvarsan is a brilliant exception. Innumerable changes have been rung on such groups as Local Anæsthetics, Hypnotics and on Salicylic Acid, valuable substances have certainly been found, the dependence of physiological action on molecular architecture has been explored and much valuable work accomplished;

they have not led, however, to discoveries of outstanding importance to Medicine. But in the actual synthesis of substances, such as Adrenalin (from Supra-renal gland), and Thyroxin (from the Thyroid), the organic chemist has been of great assistance to the physiologist and the physician in his examination of the endocrine apparatus. The replacement of dried glands by the pure substance itself means that the dosage is much more exact and the effects more to be depended on.

I have sketched very briefly the progress of knowledge during the past fifty years, based on the conception of Valency; the success in this domain has been so great that many are convinced that we are masters of these problems, and that in the course of time we shall be able to prepare synthetically any product of Nature. But I am inclined to think that a halt has come in this progress, and that we now await the discovery of the methods employed by Nature, so very different from those used in our laboratories. With the discovery of these methods a new Organic Chemistry will arise, the importance of which to Medicine, nay, to mankind in general, will be immeasurably greater than the old.

Up to this point I have pictured the application of Chemistry to the problems of Biology from one point of view only, namely, that of Molecular Architecture, and indicated the attempts that have been made to determine the structure of those complex substances, and the further problem of their actual synthesis, the second complementary to the first.

But there was one aspect of this general problem entirely omitted from consideration; that is, the question of Energy. Since no chemical reaction takes place without energy changes, it is clear that this factor is equally important, nay, essential for the full understanding of the reactions of the living cell.

As a theoretical weapon the Molecular Atomic conception of matter is incapable of assisting us in the interpretation of energy changes, but I have already mentioned that the system called Thermodynamics, independent of any theory of matter, and elaborated in the early fifties, was ready for use in the realms of Chemistry.

Willard Gibbs, Professor of Mathematics at Harvard, showed most clearly in 1874 the possibility of the application of Thermodynamics to chemical phenomena. His work marked an epoch as important as that of Lavoisier, and it is not going too far to state that Gibbs is the greatest scientist that America has yet produced. Gibbs's treatment of the subject was mathematical, and chemists, as a rule, were non-mathematical; and it was not until the eighties that Van't Hoff and many others used this process of reasoning as one of the ordinary weapons of the science.

And at this stage there appeared that unfortunate name of Physical Chemistry; and again in order to date episodes I shall give you the year 1890, in which Sir J. Walker published the translation of Ostwald's *Outlines of General Chemistry*, and familiarised English chemists with this new method of treating chemical phenomena.

I use the word "unfortunate" advisedly, for it led the uninitiated to think that it was a new branch of Chemistry, when it was nothing more than the application of new methods to the phenomena of the science. It looked upon these phenomena with new spectacles, and these new spectacles revealed a new world, and literally gave birth to a new Chemistry.

The study of chemical reactions, interpreted by Guldberg and Waage between 1864 and 1879, by means of the Kinetic Molecular Hypothesis, had resulted in the recognition of one of the most fundamental principles of Science—the so-called Law of Mass-action. The relative mass of substances

present in unit volume entering into a chemical reaction influences the proportion of the various products of that reaction. Reactions may cease before all the substances on one side are converted into substances on the other—as we would represent the reaction in a chemical equation. The whole system comes into a state of what is called Chemical Equilibrium. A reaction, indeed, may be reversed by changes in the concentration of the reacting bodies. The law was deduced, the effect of varying the amounts of the interacting substances could be calculated, but nothing was revealed as to the effect of altering the temperature, nothing as to the energy that could be obtained from such a reacting system.

The application of Thermodynamics to this problem gave the complete picture, and showed that Guldberg's and Waage's discovery was but a special case of a general theorem.

Here, then, was a new weapon for the investigation of chemical reactions and for the study of chemical affinity, and the application of these conceptions showed that the forces which bring about Chemical reactions and those which bring about the so-called Physical reactions, such as Solution, or the change of ice into water or water into steam, are all subject to the same laws and can be measured in the same way. With the study of equilibrium the idea of continuity entered Chemistry and transformed the science. And although we have certainly no such simple and universally important law such as Newton's for all the complexities of chemical phenomena, we do possess a number of universal natural laws which make possible a formal description of the course of a reaction.

Until the introduction of these conceptions Bio-Chemistry consisted of a great number of descriptions of different products accompanying living organisms, their properties, their percentage composition, in some cases their use, in

some few cases the arrangement of the atoms in their molecules. But even this quantitative element—the determination of the relative amounts of the elements present—was lacking in cases where the substance investigated occurred in such small amounts that isolation in the pure form was impossible.

Unless the newer methods of Chemistry—to which I am now alluding—be employed, the old classical science could but indicate the occurrence of such substances, their mode of preparation in the most concentrated and purest possible form, and in such condition enumerate their characteristic properties.

But the new methods made it possible to form an opinion on the manner in which they react and thereby gain a clear scientific insight into their nature.

Remember that most of those substances, such as Enzymes or Toxins, are so unstable that their solutions cannot be heated to 60°C., that in many cases they are destroyed by acids or alkalis, and that often they cannot be separated from the albuminous substances which accompany them. The new Chemistry allows us to follow quantitatively the influence of temperature, or of foreign substances upon these interesting organic products of vital importance to the physiological processes of daily life, in disease and in therapy. The value of such methods in that branch of Medicine called Immune-Chemistry must be obvious.

The influence of temperature on the velocity of different processes in which Enzymes take part, or organic products such as egg white, or living cells such as blood corpuscles, bacilli, or such higher organisms as eggs or plants, has been proved to follow the same law as is found for the influence of temperature on ordinary chemical processes.

The quantitative laws of Chemistry have been found to hold when life processes in which not simple cells, but

higher organisms are involved—as, for instance, in the experiments on the digestion of food by dogs. The data regarding digestion, secretion and resorption in an animal's body show a great number of very simple regularities, the existence of which in such " vital " processes—which depend to a high degree on psychical effects—was deemed impossible.

Experiments with trypsin, diphtheria toxin and anti-toxin, cobra poison and its antibody, again show that the same laws are valid for the equilibrium in which antibodies and antigens enter as for the equilibria studied in general Chemistry.

The quantitative determination of those equilibria leads to the conclusion that the antibodies are not analogous to enzymes or catalysts—as was often maintained—but really take part in the equilibrium.

The study of such actions throws much light on the progress of illness produced by micro-organisms, and it is a promising feature that the content of antibody during and after illness can be treated in a strictly quantitative manner, and that it has been found possible to subject this extremely important phenomenon to calculations which agree as well with the observed facts as with ideas conceived for the explanation of other parts of natural science.

The new methods enabled us to investigate chemical processes in which simple cells—such as yeast cells, blood corpuscles or bacteria—act upon or are treated with chemical reagents, processes such as fermentation by yeast cells, hæmolysis by means of hæmolytic poisons, the agglutination of bacilli by agglutinins, and the killing of bacilli by those poisons called disinfectants. All these are processes with which the old classical Chemistry was incapable of dealing.

Solutions.—Many of the phenomena resulting from the solution of substances in a pure solvent were discovered,

lost and rediscovered several times during the latter part of the eighteenth and early part of the nineteenth centuries. But it was not until much later that Van't Hoff, in 1887, offered an explanation of the phenomena in terms of the Kinetic Molecular Theory and of Thermodynamics.

You will remember that according to Avogadro equal volumes of gases at the same temperature and pressure contain the same number of molecules; or, any kind of molecules enclosed in equal volumes show the same pressure at the same temperature.

Van't Hoff extended this conception to solutions; all dissolved substances produce upon a membrane which prevents their diffusion, but a membrane through which water can pass, an Osmotic Pressure equal to that which would be produced by gaseous matter containing the same number of molecules in the same volume. Or, in solution the same number of molecules of any kind of matter produce at the same temperature and volume the same pressure on the walls which prevent their diffusion.

Living cells are surrounded by such walls—semi-permeable diaphragms—and Osmotic Pressure regulates the exchange of water between cells and tissues and the liquids of the animal body.

This means that the exchange of water between the tissues and liquids of the body can be expressed by Van't Hoff's theory of Solution, that a typical life phenomena is reduced to a fundamental chemical law.

There arises the extremely interesting question of dead and living cells considered as semi-permeable membranes. The living cells of the kidney can concentrate urea from 0.04 per cent. in the circulating blood to 2 per cent. in the urine. Such cells, in fact, appear to act in the opposite manner to dead semi-permeable membranes, and there are those who draw the inference that here there is a form of

energy and energy transformer at work which has not been observed elsewhere than in living cells.

Closely connected with Osmotic Pressure of Solutions, and capable of being calculated from it, but much more easily determined experimentally, are (1) the lowering of the freezing point, (2) the rise in boiling point, and (3) lowering of vapour pressures.

Our conception of the nature of Solutions was extended by Arrhenius in 1888, as a result of the investigations made on the passage of electricity through solutions, and of a study of Osmotic Pressure of such solutions, together with these related phenomena.

These substances, which on solution enable that solution to conduct electricity, consist not of molecules, but of molecules broken down into highly-charged atoms, or groups of atoms, termed Ions ; the extent of this breakdown can be calculated from the conductivity of such solutions, by the determination of their Osmotic Pressure, or by those other related phenomena I have mentioned, or indeed by purely chemical considerations.

All acids showed one set of properties in common, because they all give rise to the same thing—hydrogen ions—when they are dissolved in water. All bases turn red litmus blue, because when dissolved they all give rise to hydroxyl ions. The old methods of the science were incapable of determining the amount of these present, that is, the real acidity or basicity of a solution. The amount of an acid or base present in a solution as determined by titration has nothing to do with the acidity or basicity of that solution, that is, its " P_H."

Water does not conduct electricity ; dissolve salt in it, and it does ; the Osmotic Pressure of the solution, the rise in its boiling point, the lowering of the freezing point, all show that there are two things present ; the molecule of

Salt has broken down to give ions of Sodium and Chlorine, and according to this conception these, not the molecules, are the carriers of the current. All chlorides give the same test for Chlorine, because they all give rise to the same Chlorine ion. And note, the extent of the breakdown of the salt molecules can be calculated by the conductivity of the solution. Here was an entirely new point of view: chemical activity could be estimated by electrical methods.

The importance of this completely new outlook with regard to the nature of solutions was clearly of profound importance to physiologists. The body consists of over 63 per cent. of water and the cell protoplasm of 80 per cent. The materials for the nutrition of the cells of the body are conveyed to them in aqueous solution; the chemical reactions which proceed in the cells take place in the same medium. The worn-out material, the result of cell action, is carried away in solution; but there is no need to emphasise the importance of this subject. I believe I am right in stating that the phenomenon of life is unknown apart from solutions.

Colloids.—The further study of solutions revealed a new type, a new subdivision of matter termed Colloidal.

Albumen, for instance, is soluble in water, but the solution shows such an extremely small osmotic pressure, and its boiling point is so near that of pure water, that either the molecular weight is enormous—that is, there are but very few molecules present—or the solution is something entirely different from that of sugar, for instance.

The use of the so-called Ultra-microscope by Zsigmondy and Siedentopf in 1903 showed that such solutions were comprised of extremely minute particles in a continual state of movement.

Since this date the great importance of this field has been realised, and in physiological chemistry and in some branches

of technical chemistry Colloids are a source of effects so momentous and specific that a new branch of Chemistry has arisen—Colloidal Chemistry—with its own technique and its own journals, devoted to the investigations, relations and laws of a fascinating branch of the science.

Enzymes.—Before concluding, I wish to say something about those substances through whose agency, we believe, all life processes take place. In 1836 Berzelius suggested that the chemical action of the living cell was aided by some such bodies as those which brought about catalytic action in the chemical reactions of the laboratory. The value of this suggestion remained unrecognised for nearly seventy years.

Biological Chemistry, as founded by Liebig and his school, occupied itself in the study of the various constituents of the fluids and tissues of the body, the products of cell activity, and the isolation of an enormous number of crystalline chemical individuals. This material, so laboriously collected and studied, together with the technique elaborated for the isolation of such substances, led—as I have indicated—to the synthesis of many of the highly complex and important constituents of animal and plant life.

About 1900 Bredig and his students, working in the Heidelburg laboratories, found methods of preparing colloidal solutions of various metals, and observed that the behaviour of these solutions was so similar to that of the ordinary Enzymes that he christened them the "Inorganic Ferments."

Not only is colloidal platinum—for instance—a most powerful catalyst showing an astonishing power of decomposing hydrogen peroxide, when present in solution to the extent of but one part per million of water, but like the Enzymes of the living cell it is found to be extremely sensitive to the action of heat and poisons. One millionth of a

milligram of prussic acid per c.c. reduces the intense action of platinum on hydrogen peroxide to half its original value. The action of one part of sulphuretted hydrogen in 300 millions of water retards that action. This restatement of the similarity of Enzymes and the Catalysts of Chemistry marked the beginning of a great advance in Bio-Chemistry, for it attracted to it the attention of chemists trained in the new conceptions of the science.

The hypothesis that catalytic action in the laboratory was identical with such enzyme action, for instance, as that which results in the oxidation and hydrolysis in the living tissue, incited chemists on the one hand to make a thorough investigation of all the phenomena connected with catalysis and the action of colloidal substances, and on the other hand it gave to Biology a scientific working hypothesis regarding enzyme action. That the vital processes of the body in health and disease are largely dependent upon the presence of Enzymes becomes more and more apparent as these processes are studied, and that the action is catalytic in character explains how such oxidations of Carbon and Hydrogen in the process of respiration and such great chemical changes as those which occur in digestion and assimilation can be carried out so rapidly and at such low temperature in the bodies of animals.

Although some chemical reactions in the laboratory give rise to catalisers during their progress, yet it is a marked characteristic of the living cell to manufacture itself the Enzyme or Enzymes it requires, and this is carried out in a manner quite unknown to us. But apart from this, there does not appear to be any specific difference between the chemistry of the inorganic and organic Enzymes. But in all cases the action of Enzymes in the living body is adapted, controlled and co-ordinated by the cell in a very wonderful fashion, and it should not be forgotten that we have no proof

that the similarity between enzyme action and that of inorganic ferments is due to similar causes.

I suppose the ultimate solution of each medical problem lies in the combined attack by a group of investigators each trained in a separate method. Specialisation in science, even in the narrowest sense, is essential to real accomplishment.

But if medical problems are to be solved in this manner, it seems to me that the scientific basis which I have endeavoured to sketch to you should be the foundation of medical studies, and I venture to think the time has come when more time should be found, even in the heavy medical curriculum, for the consideration of those fundamental principles upon which Medicine only can rise to the status of a Science.

That the technique of the science can be mastered is not possible, neither is it necessary, I think, to over-emphasise the value of Organic Chemistry, but what is essential is a thorough understanding of the new armoury of the Science.

INJURIES TO THE HEAD ILLUSTRATING FUNCTIONS OF THE CORTEX.

BY

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THE whole subject of cortical function is beyond the scope of a single paper, and all I shall attempt to do is to illustrate some of the recent work on the subject from cases which have recently come under my observation.

To begin with, it must be remembered that the nervous system should be thought of as a hierarchy of arrangements

of neurones all modelled on the simple reflex arc. This is true whether we consider this arrangement from the point of view of structure, that is to say, receptors, central neurones, muscles and glands; or of physiological function, which involves reception of stimulus, activation of neurones, muscular or glandular activity; or of the psychical accompaniments of these, namely sensation, perception, feeling and desire. At any level in this hierarchy we find that a pattern of neurones and their connections such as that described above controls analogous patterns below it in the scale, and is itself controlled by analogous patterns above it.

Sherrington[10] showed how the nervous system may be divided into two very distinct parts. Firstly, that subserving the response to those stimuli which required intimate contact with the body to register their impression, such as touch, pain, heat and cold, etc. This is the spinal part, comprising the spinal cord and brain stem. Secondly, that subserving the response to stimuli acting at a distance, *i.e.* light, sound, and (with certain reservations) smell. This part is the brain proper. Of this latter part phylogenetic and ontogenetic evidence shows us that the cerebral cortex constitutes the newest, most complicated and highest series of patterns in the hierarchy.

Recently Bianchi[1] has shown that of the cortical areas the frontal lobes contain the patterns which integrate and control the others. Another aspect is, however, of importance. If the various areas in the cortex are examined six layers of cells may be discovered[7] making up the superficial layer of grey matter, and there is considerable evidence to show that, at any rate so far as local function is concerned, the function of the superficial layers is to control that of the deeper ones.

Rivers,[8] Head,[3] Sherrington[11] and others have very clearly demonstrated how the function of a lower pattern

is modified by that of higher patterns. It may be altogether suppressed, so that no trace of its activity is disclosed until it is released by interference with the activity of all higher patterns. An example of this is afforded by the discovery by Head and Riddoch [5] of the mass reflex in cases which recovered from complete division of the spinal cord. This reflex consisted in the response to a stimulus of the foot or any part of the leg by flexion, sweating, and voiding of the bladder and rectum. Such a reflex may be very useful to certain molluscs such as the squib, but is of no use to man. Or the function of the lower pattern may be fused with that of the higher, so that it forms an essential part of that function. An example of this may be seen in the maintenance of normal muscular tone, which is profoundly disturbed if the function of the lower pattern is interrupted by lesions of the lenticular nucleus, though the higher cortical pattern is intact. This state of affairs is seen in paralysis agitans and allied diseases.

A factor of great importance to remember when considering this hierarchy of patterns is that as we rise in the scale not only do the patterns increase in complexity but also in delicacy of adjustment, so that (if one may be permitted a hyperbole) a crowbar is needed to disturb function at the bottom of the scale but an angry word is sufficient at the top.

Another function of the cortex which must be realised is the so-called retention of memory, which involves the power of recalling images. Suppose a group of stimuli affects the brain; for example, the light waves from a tree impinge upon my retina and are conveyed to my occipital cortex, my experience is that I see the tree, but the activation of these various neurones which takes place does not leave them the same as before. What is called an engraphic effect [9] has taken place, and that particular arrangement of neurones tends to react in the same way in future in response to similar

stimuli. In this way images of the tree may be aroused, irrespective of the actual presence of the tree. It is the function of the cortex to correlate any given sensation with revived images of similar sensations, and so to give meaning to the whole and enable us to exercise what is called perception. This involves discrimination and integration of the images and sensations. It is the function of the cortex, then, to receive impressions from those sense organs reacting to stimuli at a distance, to correlate all sensory messages with images of both similar and dissimilar sensory impressions, and to discriminate between them, thereby permitting reference in time and space; it exercises control over the functions of lower levels in the hierarchy; and, finally, here are integrated all impressions in such a way as to subserve the intellectual life of the individual and to discriminate and control efferent impulses so as to allow of the most delicate manipulative activities.

The object of this paper is to try to illustrate these functions by reference to the effect of injury of the superficial cortex in the occipital lobe, the sensory area, the motor area and the frontal lobes.

The Occipital Lobe.—The first case was that of a man who suffered a severe blow on the back of the head from a fall from a lorry travelling at a high speed. The injury, which was probably a subdural hemorrhage, had involved the whole of the area of the visual cortex on both sides, with the result that he was completely and hopelessly blind; but as the mid-brain centres for muscular movements were uninjured there was no ophthalmoplegia. In other words, the more distal part of the optic tract was intact. This illustrates the function of the cortex as a receiving station for sensory impressions acting at a distance.

The second case was that of a man who was injured by a gun-shot wound on one side only, resulting in the patient suffering from a homonymous hemianopsia. This illustrates the principle that we shall find more evident later, that the cortex has to do with physiological function rather than anatomical structure. Thus the left occipital cortex has to

do, not with the right eye, but with the perception of stimuli coming from the right side ; just as we shall find that the motor cortex has to do with movements and not with anatomical muscular groups.

The third case was one of a large gun-shot wound on the lateral aspect of the occipital lobe, which must have caused injury to a considerable area of the cortex, though it did not involve the actual visual area. This man had been a ship's purser, and had travelled widely, knowing several languages. He still retained considerable intelligence, and so his condition was easy to investigate. Before the injury to his brain his visual imagery had been extremely accurate and vivid. Now it was with the greatest difficulty that he could give any description of what to him had been a perfectly familiar sight, namely the rock and harbour of Gibraltar. He had only a vague idea of the shape of the rock, and could get no picture of the sweep of the bay or where Algeciras lay. Even such a familiar object as Clifton Suspension Bridge was described but vaguely, with no detail whatever. His languages were very much impaired as to vocabulary, though his accent, which depended on auditory imagery, was fair. This illustrates the function of the cortex in revival of images.

A fourth case was that of an epileptic whose fits dated from the age of six, when he sustained a severe injury of the right temple. At times the ordinary attacks of grand mal and petit mal were replaced by what are called visual equivalents. In these attacks there appeared before his eyes lights or sometimes figures which started in the centre of the field of vision and passed over to the right margin of the field. While these were going on he had a right homonymous hemianopsia, which passed off with the end of the attack. Here there was suppression of the proper highest function of the visual cortex at the left occipital pole with substitution or liberation of lower and less co-ordinated function. This corresponds exactly with what happens in lesions of the motor cortex which cause fits. The cause of these attacks is doubtful, but I venture on this explanation. At the time of the blow there was a disturbance at the opposite occipital pole by contre-coup, which injured the superficial cells of the left occipital lobe, so that under certain conditions their function was entirely abrogated, and the activity of deeper and lower grade cells was liberated.

In this connection a result of less severe occipital lesions cannot escape notice. That is the frequency with which typical migrainous attacks are initiated by such an injury. These are associated with a visual aura followed by headache,

and the analogy with the visual epileptic equivalents described above, is at least permissible. I would suggest that these attacks of migraine depend, at least partially, on an interference with the highest grade superficial cells whose function it is to control the activity of the lower; further, that a liability to migraine depends on an instability of these highest grade occipital cells, just as an epileptic fit depends on an instability of the highest grade cells of the motor cortex. This, of course, does not explain the onset of any individual fit or attack of migraine, but only the tendency of the patient to suffer from them.

As to the discriminative function of the occipital cortex, this is probably concerned with colour vision. It is a matter of common knowledge that savages are often unable to discriminate between different shades of the same colour, and the same applies to many low-grade intellects in civilised communities. Presumably colour blindness may have something to do with congenital interference with this discriminative function where the receptive end organs are intact. I am not aware that any exact observations have been made on colour discrimination in connection with injuries to the occipital cortex. Holmes [6] described a doubtful case of achromatopsia with retention of the field for white, but drew no conclusions from it. However, if we remember that the higher discriminative neurones have their projection fibres proceeding from the periphery, and that the highest grade cell and fibre are always affected first in any disease process, it is a significant fact that in pituitary tumours a hemiachromatopsia often precedes hemianopsia. More work is needed on this point, which seems to have escaped the attention of neurologists and ophthalmologists.

The Sensory Area.—In the fifth case, which is illustrative of a large group of head injuries, there was a wound in the parietal bone over the post-central gyrus where the sensory

area of the cortex is situated. We find that quite a small area of the body is affected, namely the right hand; that the patient complains of no pain, but states that he has a "paralysis" of his right hand. When we examine him, however, we find there is no paralysis and that the muscles work all right, with certain reservations. If both hands are stretched out in front of him there is a slight drooping of the right; he has a mild degree of hypotonia which is really due to false co-ordination. If he is asked to perform certain movements requiring manipulative dexterity, such as opposing the thumb to the other fingers in succession, picking up a pin or doing up a button, he is hopelessly at fault. If we examine his sensation we find he can appreciate pain, extremes of heat and cold and touch, but he cannot localise where the stimulus was administered with any degree of accuracy, nor can he discriminate the exact nature of the stimulus, and above all he has no idea of the position of his hand or fingers. He shows partial astereognosis, and fails to distinguish between the different textures of materials, such as silk and cotton. The result of all this is that, in spite of appearances, he has a very inefficient hand, and except for steadying things he might just as well be without it.

To explain why such a state of affairs is met with we must consider for a moment the physiology of the sensory paths. All the various forms of common sensation are subserved by special end organs in the skin and deeper parts, but all similar sensory paths are quickly grouped together in the spinal cord. Those for pain, heat and cold and certain touch fibres pass to the opposite side of the cord and travel up the lateral columns to the corresponding optic thalamus. The fibres concerned with posture, discrimination between two compass points and the rest of the tactile fibres proceed up the posterior columns of the same side to the nuclei of the fillet in the medulla. Thence fibres cross to the opposite side and travel to the optic thalamus. Here, then, all sensory fibres from the opposite side of the body meet once more at their second cell station within the central nervous system. Thence the sensory impulses are redistributed. All or almost all sensations have two aspects, a discriminative

and an affective aspect. By the first we mean the reception of the information which would answer the questions, Where in the body was the stimulus applied which gave rise to this sensation ? What sort of a sensation was it ? and What sort of a thing caused it ? By the second or affective aspect we mean the reception of information telling us what it feels like, was it pleasant or unpleasant ? Head [4] has shown that this latter affective aspect is dealt with by the lateral nucleus of the optic thalamus, while the former discriminative aspect is dealt with by the cortex. It is obvious that such a sensation as posture has little or no affective aspect ; for instance, it is not specially pleasant or unpleasant to have one's fingers bent or straight, and correspondingly this sensation is not represented in the thalamus, nor affected in lesions of this. On the other hand, such a sensation as pain is almost entirely affective, and in consequence it is not represented on the cortex to any extent, and in lesions of this part pain is not interfered with. The lateral nucleus of the thalamus may be regarded as the highest station in connection with pain, and this, of course, is not easily influenced by any means physical or psychical. That is why once a real habit of pain has been established it is so extremely difficult to get rid of, though in less severe cases functional pain may be readily removed.

The sensory cortex subserves five functions : (1) the recognition of posture and passive movement, (2) the recognition of certain tactile elements ; (3) the appreciation of two points applied simultaneously to two different points on the surface of the skin, and also the recognition of the size and shape of objects which are in contact with the skin (spatial discrimination) ; (4) the localisation of the situation of a stimulated spot on the skin and the recognition of two consecutive stimuli (discrimination of time) ; (5) the recognition and discrimination of a scale of sensations with heat

at one end and cold at the other. In addition, it is the function of the cortex to relate one sensation with another. We see that these functions correspond to the deficiencies exhibited by the patient whose case is described above. Graham Brown and Stewart[8] experimented on the retraining of tactile localisation on such a "sensory" hand, and met with considerable success. Personally, I have not had the opportunity of carrying out retraining experiments with such exactitude as they did, but in my experience something can be done by re-education in restoring the use of the hand and a little in restoring the sense of position.

The Motor Area.—It is not necessary to say much about the motor cortex, which is situated in the precentral gyrus, because injuries in this area are productive of the most obvious effects, which are familiar to everyone. It should be noticed that even in cortical injuries the motor symptoms are often complicated by sensory deficiences due to injury of the adjacent sensory cortex; and in the vascular lesions so common in civil life, in which it is the subcortical fibres of the internal capsule that are affected, the sensory fibres are almost always damaged at the same time. So far as the motor symptoms are concerned we notice two main features, an alteration in tone and a special type of paralysis. The first is an increase in the normal tonic contraction of the muscles. This phenomenon has been definitely shown by animal experiment to be due to liberation of lower motor systems which are more concerned with posture than locomotion, hence the rigidity of the lower limbs in extension. The rigidity of the upper limbs in flexion is peculiar to man, and is perhaps suggestive that in his less remote ancestry this lower motor system was already adapted to hanging on to the branches of trees, at least with the arms. So in this alteration of tone we have an excellent example of the controlling and integrating functions of the cortex, for when

the latter is intact this postural function is relegated to its proper place, and in no way interferes with the more delicate and important function of locomotion. Secondly, as regards the paralysis, we find on examination that there is no complete loss of motion, though certain movements are impossible, nor is there a complete paralysis of one group of muscles as is the case in lesions at lower levels. This shows us, firstly, that the motor function when at the cortical levels is concerned with movements and not with muscles, or in other words that an integration of individual muscular actions with a proper correlation between agonists and antagonists has taken place. Secondly, if we examine the movements which are possible we discover that the limb moves as a whole, and that the more distal the joint the less independent movement is possible. This illustrates the function of the cortex in allowing discriminated movements, especially of a high grade manipulative type, so that we may presume that the accomplished pianist is one who is endowed with a particularly finely-developed motor cortex in the hand area, but he also requires an adequate associative connection with his frontal lobes, and through them with his temporal lobes, if he is to correlate his finger movements with his auditory images of notes, for they are the final and highest integrative station.

A few words may be said here as to fits. Seizures due to trauma must be divided into two classes. Firstly, there is traumatic epilepsy, in which the fits resemble those of ordinary epilepsy with no definitely localising symptoms. These may develop up to two years after the injury, and tend to persist, though there may be remissions. They occur after injury in any part of the head, but most commonly after parietal injury. Thus Aldren Turner[12] describes a series of 38 cases in which 10 had frontal, 16 parietal, 9 occipital and 3 temporal lesions. As Hughlings Jackson and

subsequent workers have shown, fits are a release phenomenon due to failure in the controlling function of higher cortical levels, and for this reason surgical intervention which is in any way concerned to interfere with the cortex itself is doomed to failure in these cases. The removal of a cortical scar which has already destroyed cortical tissue and allowed fits to develop will only destroy more cortical tissue and so make the fits worse, and such procedures, though all too common in earlier years, have now been given up. In traumatic epilepsy surgery has little or no place, and even such operations as filling up gaps in the skull are apt to increase the number of fits or even produce them as a new symptom.

The second class is the focal or Jacksonian fit, which always begins in some localised part and may or may not progress to complete unconsciousness. Such are due to so-called "irritation" of the motor cortex by a serous or blood cyst or spicule of bone, and come on soon after the injury. If such fits cease, as they may do, spontaneously they do not tend to recur, and they may be cured by surgical intervention to remove the source of "irritation." If, however, we retain this word irritation we must understand what we mean. The spicule of bone does not irritate the motor cortex as an electric current irritates and sends an impulse through a nerve muscle preparation, but it may produce a localised œdema whereby several cortical cells are thrown out of action, and their controlling action being removed, fits are able to occur. Removal of the local pressure allows the cortical cells to resume their function, and so re-establish control.

The Frontal Lobes.—This area of the brain is often described as silent; that is to say, injuries to these lobes do not produce any obvious effects. If by obvious effects are meant paralyses and sensory changes, as a rule there

are none of these, but more careful investigation does elicit changes which have taken place as the result of severe frontal wounds.

I may here quote a case of a severe wound over the frontal lobes as illustrative of many. The wound was mesial in position and involved considerable destruction of brain tissue. We find the man suffering from no paralysis or sensory defects, but in certain respects he is considerably incapacitated. For example, his power of recall is very deficient, and he has great difficulty in remembering when things happened, so that in taking his history he is continually antedating and postdating his events. In other words, his power of reference in time is seriously affected. Still more, his power of correlation of ideas is at fault. He cannot grasp a story as a whole. Even in conversation he gets confused unless the statements made to him are simple and direct, yet before his wound he was an intelligent man with a good record. At the same time he has difficulty in controlling his emotions, he laughs or cries easily, loses his temper readily. If not specially aroused he is dull and apathetic, does not notice things about him, and will not readily take initiative over anything.

Such symptoms are not uncommon in all injuries to the head, but they are less definite and less persistent after wounds of other areas.

Let us turn now to the description of monkeys whose frontal lobes have been removed in the experiments carried out by Professor Bianchi,[1] who has done so much to elucidate the function of these higher parts of the brain. He finds that they show defects of perception, and of discrimination between objects with superficial resemblance; thus they cannot distinguish between threat and reality, and so become to a large extent incapable of play. They also display deficient observation, objects which would be investigated by the normal monkey being overlooked. Memory is defective, so that past experience is not utilised, and they do not learn by experience. Associative power is greatly reduced, so that there are no

new adaptations. Judgment is poor and immediate. There is a lack of initiative and one movement does not lead to another; thus a monkey will seize a door handle (stimulus of bright object), but will not proceed to turn it. The primitive emotions remain, the desire for satisfaction of hunger, thirst and other organic needs, and especially that irrational, illogical fear which seems to have no definite relation to stimuli; but higher sentiments, such as friendship, gratitude, jealousy, maternal protection, dominion, authority, self-esteem, ridicule and, above all, that of sociality, disappear. Conduct is incoherent and stereotyped actions and tics are often present.

We see in the symptoms complained of by the man described above many of the characteristics of the monkeys, and they are symptoms which, though not obvious to the casual glance, are a real hindrance to anyone in the work of the world, and require to be carefully considered if an estimate is being made of such a patient's capacity to undertake employment. As was said at the beginning, the stability at these high levels is very delicately balanced, and it does not need a gun-shot wound to disturb the functions of the frontal lobes. It is a well-established rule in neurology that the most recently acquired functions and latest developed structures suffer most severely from injury or disease and probably in most cases of concussion it is the frontal lobes which suffer the chief damage and which take longest to regain their functional capacity.

The description of Bianchi's monkeys would do very well for a neurotic patient, and there can be little doubt that many of the symptoms of the neuroses are due to a functional dissociation of the frontal neurone control. The possession of well-developed frontal lobes undoubtedly allows of man's greater adaptability to the environment and elasticity of response to stimuli as compared to the animal, and we may

recognise in certain savages and many defects obvious characteristics which are unquestionably due to defective development of these. In the neurotic there is no lack of development of the higher levels, but from dissociation, presumably at synaptic junctions, control is abrogated and certain functions of lower levels are allowed to express themselves unchecked, while other higher functions are split into their component parts, so that they no longer subserve a unified pattern of behaviour. However, these speculations as to the physiological explanations of the neuroses hardly have a place in this paper, whose purpose is to illustrate by the cases of injury which have been quoted the five great functions of the cortex, namely reception of stimuli acting at a distance, control, integration, discrimination and reference in time and space.

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[12] Turner, W. Aldren, " Epilepsy and Gunshot Wounds of the Head," *J. Neurol. and Psychopath.*, 1923, iii. 309.

HOARSENESS: THE IMPORTANCE OF EARLY LARYNGOSCOPY.

BY

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HOARSENESS which lasts beyond quite a few days demands an examination of the larynx; clearly this part is affected whatever the condition elsewhere. When transitory this symptom is usually of slight importance, but when persistent it cannot be lightly regarded. Especially is this so when hoarseness is the sole trouble. "Hoarseness alone, without pain or any other symptom, may be the only portent of an early tuberculosis, laryngeal cancer, tabes dorsalis, aortic aneurysm or other affection, foreshadowing the urgent need of vigorous therapeutic measures."[1]

CASE 1.—**Aneurysm.** G. H. H., male, æt. 50, clerk. Came to me in October, 1922, complaining of hoarseness of three months duration, without any other symptoms; onset was sudden, not associated with any disturbance of general health.

Examination.—Paralysis of left vocal cord, nothing else abnormal. Careful clinical examination failed to elicit anything to explain this, but a skiagram showed aneurysm of the aortic arch.

The examination should be early, quite at the beginning of the trouble. As soon as it becomes clear that the hoarseness is not rapidly clearing up we must seek if possible an explanation, before progress of disease has produced other signs indicative, perhaps, of irreparable damage. Indirect laryngoscopy is painless and simple; even children, if docile, can be examined without trouble—my youngest

patient this year was only four years old. Yet this essential inspection is sometimes quite unaccountably deferred.

CASE 2.—**Trauma of Larynx.** A. P. R., male, æt. about 30. Complains of hoarseness since being wounded in throat four years earlier. The bullet had been removed by operation. Voice only hoarse whisper with periods of complete aphonia.

Examination.—Left vocal cord entirely missing. Left arytenoid fixed. Right side almost normal. This patient said he had been having treatment by suggestion, etc., for over two years for functional aphonia. Further treatment not advised.

Admitted that this instance is exceptional, yet it seems not very uncommon for examination to be delayed for a considerable period.

The eight remaining cases are examples from those which came under my care during the first four months of this year. In all hoarseness had been present for quite a long time before the larynx was examined; in several this was only done because further symptoms appeared. The notes of each case indicate for what reason an early examination was important.

CASE 3.—**Granuloma of Larynx.** Fig. 1. F. B., male, æt. 35, labourer. Complains of hoarseness four years, following exposure to mustard gas. No pain, recently periods of aphonia, increasing dyspnœa on exertion. Hoarseness severe and increasing.

Examination.—A greyish-pink, smooth, faintly lobulated mass, attached to anterior subglottic region, coming between cords on expiration. Diagnosed "fibroma." I removed the tumour by endoscopic operation. It measured about half an inch each way, and on section proved to be a granuloma. This patient had been for over a year having treatment for "D. A. H." He was shown to the Medico-Chirurgical Society before operation (February, 1923) and after, when the voice was good and the man very satisfied (April).

CASE 4.—**Hypertrophic Laryngitis.** Fig. 2. P. P., male, æt. 28, miner. Complains of hoarseness four years, getting worse; attributed to exposure; no other trouble except dysentery in the past.

FIG. 1, CASE 3.

Granuloma of larynx. A greyish-pink faintly obulated mass, attached to anterior subglottic region (p. 154). Deep inspiration.

[All the illustrations represent appearances on *indirect* laryngoscopy.]

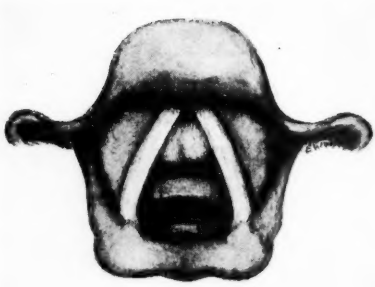


FIG. 2, CASE 4.

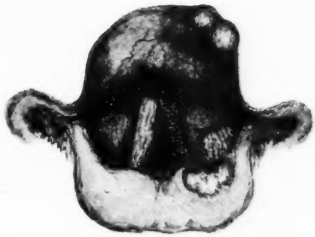
Hypertrophic Laryngitis. On left vocal cord two prominent white horns. On right cord and posteriorly also on left, infiltrated areas. Elsewhere scars of old ulceration, some recent ulceration. Posteriorly some subglottic œdema (p. 154). Deep inspiration.

FIG. 3, CASE 7.

Carcinoma of right vocal cord, almost entirely hiding the cord. Right arytenoid and false cord are fixed. The growth was found to extend into aryepiglottic fold (p. 155). Deep inspiration.

FIG. 4, CASE 8.

Tuberculosis of larynx. Ulceration of left false cord and arytenoid region and of left vocal cord. Injection of right vocal cord. Inflammation and tubercle formation (very large) of epiglottis. Œdema of arytenoid and cricoid regions. Quiet respiration (p. 155).



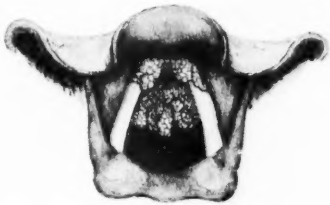
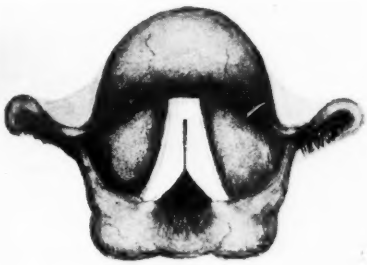


FIG. 5, CASE 9.

Papilloma of larynx, attached anteriorly, mainly subglottic but involving both vocal cords. An "infantile" epiglottis. Deep inspiration (p. 156).

FIG. 6, CASE 10.

Functional aphonia, anteriorly traumatic web between cords. Position on attempting phonation—inter-arytenoideus paresis, with hyper-inversion of abducted arytenoids (p. 156).



Examination.—A most extraordinary larynx. Two large white horns on left vocal cord impinged on phonation on a dull red semi-pedunculated mass of granulations on the right. Farther back old and recent infiltration and ulceration caused extensive deformity of the cords. Wassermann negative. This man had received no benefit from a course of several months of inhalations, etc. Operation declined.

CASE 5.—**Syphilis of Larynx.** R. O'M., male, æt. 48, seaman. Complains of hoarseness for "a good time." During last six weeks severe, with pain on speaking and on swallowing. Pale, thin, weak, ill.

Examination.—Both vocal cords red, swollen and ulcerated. General œdema of arytenoid regions and cricoid. Wassermann strongly positive.

There were no other signs; a completely negative history. On galyl and iodide the larynx healed completely, but with some permanent damage.

CASE 6.—**Laryngeal Tuberculosis.** W. C., male, æt. 24, quarryman. Complains of hoarseness nine months, getting worse. Pain on swallowing recently, none on speaking. Cough and sweating at night. Wasting.

Examination.—General congestion of larynx. Deep ulceration of right false cord and left aryepiglottic fold. Right vocal cord slightly ulcerated posteriorly, left shows infiltration of corresponding region. Diagnosis: tuberculous laryngitis; Wassermann negative; sputum swarming with tubercle bacilli; old and active tuberculosis of both lungs. Prognosis very bad. This man had been having medicine for sore throat for five months, and was living with wife and two small children.

CASE 7.—**Carcinoma of Larynx.** Fig. 3. W. H., male, æt. 50, labourer. Complains of hoarseness four months, recently slight pain on speaking; a little hoarseness for several months previously.

Examination.—Right vocal cord almost hidden by a reddish nodular growth with slight tendency to ulceration. Right arytenoid fixed, false cord rather full. No glands. Pathological report, "Squamous carcinoma." At the operation I had to remove all the right half of larynx within the ala of the thyroid cartilage, including the arytenoid. So far he has done well (third month). If this man had come under treatment earlier the operation would have been simpler, the risks less, and the prognosis as regards recurrence better.

CASE 8.—**Laryngeal Tuberculosis.** Fig. 4. S. L., female, æt. 24. Complains of hoarseness with cough ten weeks.

Sore throat six weeks. Recently pain on speaking or swallowing, much expectoration. She is weak, thin, wasting.

Examination.—Deep ulcers of left aryepiglottic fold and false cord; left vocal cord bright red, raw; epiglottis swollen, crimson, showing two large tubercles near margin; mucosa generally pale and œdematous. Diagnosis, tuberculosis of larynx, sputum negative. Marked signs in right pulmonary apex and elsewhere. This woman had been having medicine for cough for ten weeks. In 1922 she had been laid up with pleurisy. She was looking after husband and three small children, was pregnant, and was literally dying of consumption.

CASE 9.—**Papilloma of Larynx.** Fig. 5. P. S., female, æt. 16. Complains of hoarseness for six years, getting steadily worse, recently some dyspnœa. When three years old she had had an operation on throat. No pain.

Examination.—An extensive papilloma springing from anterior part of larynx, mainly subglottic but involving both cords and coming between them on attempting phonation; more than half the glottic aperture is obstructed.

The bulk of the growth I removed by endoscopic operation; the remainder is being dealt with; the larynx has probably suffered irreparable damage as the result of the parents' neglect.

CASE 10.—**Functional Aphonia.** Fig. 6. H. J. S., male, æt. 40, labourer. Complains of hoarseness since an operation for removal of bullet in larynx in 1918. Told then that he would never recover voice; has hoarse whisper.

Examination.—Larynx practically normal; a web unites anterior ends of vocal cords, but does not interfere with perfect movements. On attempting phonation the arytenoids are adducted (normally) then abducted and hyperinverted; interarytenoideus paresis, a stigma of functional trouble.[2] Under ether he phonated.

Diagnosis: functional condition with organic basis. Treatment declined. Prognosis at this late stage doubtful.

I am indebted to Mr. J. P. I. Harty, F.R.C.S., for permission to use the notes of Cases Nos. 6, 7, 8 and 9.

REFERENCES.

[1] P. Watson-Williams, "Clinical Import of Hoarseness," *Practitioner*, 922, cviii. 154.

[2] P. Watson-Williams, "Diseases of Upper Respiratory Tract," 1894, p. 167.

Reviews of Books.

Elements of Pharmacy, Materia Medica and Therapeutics. By Sir William Whitla, M.P., M.D., Etc., 1923. Eleventh Edition, 47th Thousand. London: Baillière, Tindall and Cox.—This excellent old friend is invaluable both to the student and to the practitioner, as it contains such an extraordinary amount of information on all three subjects. Indeed, we know of no other work at once so comprehensive and so exact. It has been again revised and brought up to date, and an immense number of non-official remedies are ably described and their claims discussed. It now includes a directory of what to do in case of poisoning, where many new remedies may be found, such as adrenalin and permanganate in strychnine and cyanide cases. In the treatment of carbon monoxide poisoning we wish that it had been said that the oxygen should be given under pressure, the open method being unreliable.

Reports of the St. Andrew's Institute for Clinical Research. Vol. I. London: Henry Frowde.—This Institute is one of the great romances of our time. Sir James Mackenzie, after a successful life, feeling deeply the difficulties in the way of the advancement of medical learning, has settled down with a little band of helpers to think out a fresh *Novum Organon*, and to revise our logical methods for the study of disease. Like his brother Scot, who prayed, "Lord, have mercy on the poverty of our art," he recognises keenly the limitations of medicine, and in place of improved chemical or other laboratory methods he looks for progress from minute observation of clinical symptoms, especially those in the earliest stages of disease, and the continuance of this watching through the entire course of the disease. Whether or no his quest will revolutionise medicine, a perusal here of his methods of case taking shows the very great amount to be learnt from the minute study of a single clinical symptom, such as pain or exhaustion. He points out that symptoms are the reaction of the tissues to the injurious agent which causes the ill-health, and that most of them are disturbances of normal reflexes.

A Manual of Surgical Anatomy. By Lewis Beesly, F.R.C.S., Edin. and T. B. Johnston, M.B., Ch.B. Second Edition. Pp. xiv., 561. London: Oxford Medical Publications. 1922. Price 18s.—This edition of a text-book which has attained to

considerable popularity, has been revised and brought up to date. It treats the subject from an anatomical point of view, and it must be admitted that the inclusion here and there of an occasional clinical case would have the effect of making it more readable. The student in his later years finds his days very full, and it is much to be doubted if he spends many hours in systematic reading of surgical anatomy ; he might be tempted to spend more if it were presented to him with its clinical bearing a little more strongly emphasised. We note with regret that the Basle terminology has been retained ; we were under the impression that it was as discredited by anatomists as it is ignored by clinicians. Certainly the student knows little of it, and even less of the classics. An examiner seeking information about " Dislocations of the Talus " would not generally receive a ready reply. War lessons receive attention especially in the matter of nerve injuries, but we should have liked to see the question of infection of the knee-joint treated differently, in the light of war experience. One thing the war taught us was that to put drainage tubes into an infected knee-joint was generally to condemn the patient to the loss of his limb, if not his life ; yet here we find precise directions for inserting numerous tubes into the joint. These are small blemishes where generally there is room for nothing but praise. Certainly the candidate for even the highest examinations can face his ordeal with confidence if he has a good working knowledge of the subject as presented to him here. The excellent illustrations, many of them in colour, deserve a special word of commendation.

De Arte Phisicali et De Cirurgia of Master John Arderne, Surgeon, of Newark, dated 1412. Translated by Sir D'ARCY POWER, K.B.E., M.B. Oxon., F.R.C.S. Pp. xii., 60. London : John Bale, Sons & Danielsson Ltd. 1922. Price 10s. 6d. net.—We owe this unique and beautiful volume to the Wellcome Museum, which came into the possession of a photographic copy of a MSS. of this treatise existing in the Royal Library at Stockholm. The treatise appears to be an epitome of one or more of Arderne's works compiled in 1412, some years after his death, for everyday use. It consists chiefly of directions for treatment and prescriptions for various conditions from flatulence to pleurisy, periostitis, and calculi. Brief instructions for the management of different fætal presentations in labour show when turning is needed and how delivery can be effected. The translation is wonderfully clear, and Sir D'Arcy Power's knowledge of Arderne has enabled him to supply missing words and elucidate doubtful passages from other writings of his. Twelve sections of the photographed MSS. are here reproduced with the quaint original illustrations.

These beautiful plates give some idea of the heavy task of Mr. Eric Millar in transcribing the text. The treatise itself does not, however, do justice to Arderne, omitting as it does so many of his *obiter dicta*, and showing little of his real surgical skill, while it embodies many popular superstitions of the time which could be gleaned from his writings. It is interesting to find among the strange remedies proposed a simple hot brick recommended for stomach ache, and to be told that wine is hurtful in every nerve complaint.

Greffes Testiculaires. Par Le Docteur SERGE VORONOFF. Pp. 83. Paris: Libraire Gaston Doiu. 1923.—This is an extremely interesting resumé of the work done by Dr. Voronoff on the effects of testicular deprivation and implantation in animals, founded on 120 experiments. He has justified these in, apparently, obtaining rejuvenating effects in the senile man by the implantation of testicular fragments from the anthropoid apes. The communication is verified by the results of retardation of sexual characteristics, by the development of characters found in the opposite sex, by regeneration of the senile animal, and by obtaining in man also apparent rejuvenation. The results shown photographically and the microscopic findings bear out his contention that the testicular hormone survives in the transplant and influences the host, and that the undeveloped testicle even tends towards full development. The book bears the stamp of honest investigation and is well worth reading.

Hewitt's "Anæsthetics and their Administration." Edited by HENRY ROBINSON, M.A., M.D., B.Ch. Fifth edition. Pp. xiii., 576. London: Oxford Medical Publications. 1922. Price 30s. net.—Dr. Robinson has successfully performed the difficult task of re-editing the popular textbook on anæsthetics written by the late Sir Frederic Hewitt, and he has obviously spared himself no trouble in seeing that every section of the work is abreast of the times. We are sorry that the Index of Authors has been omitted. The new account of the Physiology of Anæsthesia written by Professor Clark will be found full of useful information described in very lucid language. The better-known theories of the way in which these drugs act are given briefly with short comments as to their feasibility. This section includes some very practical references to the influence of anæsthetics in the production and prevention of shock. Dr. Robinson is a strong advocate of nitrous-oxide and oxygen, also of spinal anæsthesia, and these two methods have received careful treatment which will be appreciated by practitioners and students alike. By so able a revision the continued popularity of this old favourite has been ensured.

Medical Report of the Tainan Hospital, English Presbyterian Mission, Formosa, 1920-1922. (For distribution among the Medical Profession only.) By JAMES L. MAXWELL, M.D., B.S. Lond. Pp. 26.—Two European medical men, working in a hospital of 150 beds, have in less than three years treated over 6,500 in-patients and over 25,000 out-patients. These are the bare facts which this short report sets forth, with details which go to show that the experience to be gained in this and similar hospitals is of the first quality. This argument, together with the urgent need for workers, may bring young graduates who are keen on their profession to consider whether the career of a medical missionary may not have its attractions. This pamphlet, which includes an extremely interesting tabular summary of the surgical work done during the period under review, may sound the " call " to some of them.

Selected passages from " De l'Auscultation Médiate." By R. THÉOPHILE H. LAENNEC, with a biography by Sir WILLIAM HALE-WHITE, K.B.E., M.D. Pp. x., 193. *Medical Classics Series.* London: John Bale, Sons & Danielsson. 1923. Price 12s. 6d. net.—It is a good thing to be called upon from time to time to remember famous men and our fathers that begat us. The *Medical Classics Series* comes most opportunely, at a time when physical examination runs some risk of being overshadowed by laboratory examination and " mail-order " diagnostics, to remind us that the men of past times made discoveries and progress no less striking than our own. Sir William Hale-White in his biographical preface to this translation gives three reasons for the immediate success of Laennec's book on Auscultation. Firstly, because it contains perfect, precise and original descriptions of clinical symptoms and post-mortem appearances. Secondly, on account of the description of auscultation with a stethoscope, which he invented on the spur of a singularly happy moment. Thirdly, by reason of the beauty of language and the economical precision of words which makes Laennec a pleasure to read. The opening words of his first chapter (on voice sounds) are strikingly reminiscent of Auenbrugger. Laennec begins, " When a healthy man speaks or sings his voice reverberates within his chest "; Auenbrugger had written nearly sixty years before : " The chest of a healthy man resounds when it is struck." From these two observations two men made out the whole art of physical examination of the chest, Laennec completing the great work that Auenbrugger had begun, with frequent acknowledgment of his debt to that master and his enthusiastic disciple Corvisart. Many books have been published for the benefit of students starting in the wards and intended to explain in simple language the difficult practices of percussion and auscultation. But for

simplicity Laennec stands above them all. Take, for example, the *crepitant râle*, which he says is the pathognomonic sign of the first stage of peri-pneumonia, "a kind of crepitation comparable to the crackling sound produced by salt heated on a frying-pan." We may well apply to Laennec his own remarks on Bayle with which he concluded his chapter on Metallic Tinkling: "It is given to no man to see everything. But what he did see, he saw superlatively well, and there are few books in which there is less that requires deleting than in his." To medical students, who may come under reproof for idle and depraved recreations, we offer as some consolation that Laennec's devotion in his youth to music, dancing and rambles in the country worried his uncle (who was one of his teachers in hospital) not a little; especially music, which he loved best.

Suggestion and Common Sense. By R. ALLAN BENNETT, M.D. Pp. 105. Bristol: John Wright & Sons Ltd. 1922. Price 6s. net.—The author, in his preface, frankly admits that he has always "shunned psychology and clung to that which is good," whatever the latter phrase may mean. The reader may be excused, therefore, if he finds difficulty in accepting the author's psychological concepts as set out in the first two chapters. In his first chapter, on "Psychology and Organic Life," he misuses the term consciousness by broadening the meaning out of all recognition. When he wishes to use the word in the accepted sense he finds himself obliged to introduce a qualification, and speak of "conventional consciousness." By what right is the physiological response of tissues or isolated cells to be termed "conscious" or "intellectual"? Can we call a phagocyte intellectual? If the author had described the phenomena of adaptation in organic life in terms of specific response or behaviour the first chapter would be full of interest and free from objection. Consciousness of the individual cell is unthinkable. The writer evidently wishes to give some description of his experiences and successes in the field of psychotherapy. In so far as he sticks to the narration of experience he is interesting, though the subjects have been covered many times before and more scientifically. The book is pleasant reading, if not profound. One is left with the impression that in the writer's estimate common sense belongs to a higher category of thought than scientific thinking.

The New Physiology in Surgical and General Practice. By A. RENDLE SHORT, M.D., B.S., M.C.S. Fifth edition. Pp. xi., 330. Bristol: John Wright & Sons Ltd. 1922. Price 9s. 6d. net.—Since 1911, when this book was originally published, several editions have appeared, so that but little of the contents of the first is to be found in the fifth. But this

work preserves its essential features, and presents a number of separate essays on those portions of physiology which are of special interest to physicians, surgeons and general practitioners. It also possesses an interest for everyone who, like the author, believes that an intimate relationship should exist between physiology and medicine. This view is not universally held, since the teaching of physiology is often controlled by those who not only have no medical qualification, but are quite unsympathetic to the needs of medical students or of medical men. This work no longer limits its interest to surgical problems and to the common everyday aspects of disease. This is easily realised when such subjects as the physiology of muscular exercise and the functions of the kidney are included. These are admirably discussed, while the diseases dependent on deficiences in foods are considered at some length. An excellent chapter on the heart, occupying some forty pages of the book, is contributed by Dr. C. E. K. Herapath. Difficult as it is to adequately show how the research work of laboratories has a direct bearing on practice, it is even harder to impress this truth. Perusal of this book, which succeeds in accomplishing what is certainly a matter of some difficulty, will show how physiological work, or rather physiological knowledge, may be considered as a science which has a direct application to medicine. Apart from this the work is full of interest, more so according to one reviewer than a novel.

The Surgical Diseases of Children. By F. C. Pybus, M.S., F.R.C.S. Pp. xviii., 408. London: H. K. Lewis & Co. Ltd. 1922.—This book meets a distinct want, as no volume of the kind has of late been published, and students are compelled to hunt through manuals of general and orthopædic surgery for any account of the surgical ailments peculiar to children. In parts the book is somewhat sketchy, and the details of operative treatment might be amplified with advantage, but the commoner conditions, with their treatment, are very clearly and concisely described. Attention may well be drawn to the author's warning against the over-preparation of children for operation. This is a very common and serious fault, and preliminary purgation and starvation are still too often employed, with disastrous consequences. In acute osteitis Mr. Pybus is able to show most excellent results from complete and partial diaphysectomy. The operation deserves to be more widely practised, as it is undoubtedly an immense improvement upon the less radical methods still commonly employed in the treatment of this disease. It may interest Bristol readers to know that the late Mr. Stack performed a complete subperiosteal removal of the shaft of the radius as long ago as 1908 with a perfect result both as regards function

and bone regeneration. Mr. Pybus's book does not pretend to be an exhaustive manual of the surgery of children, but is based almost entirely upon his own personal experience and practice, and as such it may confidently be recommended. The senior student desirous of obtaining some special knowledge of a very important branch of surgery will find this very readable and up-to-date little book particularly valuable.

The Sympathetic Nervous System in Disease. By W. LANGDON BROWN, M.D., F.R.C.P. Second Edition. Pp. xi., 161. London: Oxford Medical Publications. 1923. Price 10s. 6d. net.—The progress made during recent years in our knowledge of this subject has necessitated the publication of a second edition within three years of the first. No higher praise can be afforded to it than to say that it retains the charm of the first edition, losing nothing in its masterly condensation of a large mass of nebulous data into a form that can be clearly surveyed by the least expert of students. It is a book that ought to be read by every practitioner of medicine, and for this reason we wish the cost of the book were not so high in proportion to its bulk.

A Synopsis of Surgery. By ERNEST W. HEY GROVES, M.D., M.S., F.R.C.S. Sixth Edition. Pp. viii., 621. Bristol: John Wright & Sons Ltd. 1922. Price 17s. 6d.—This book was bound to succeed. It is so full and yet so handy; it gives such a wealth of information at a glance, and is written with such discretion, that it is no matter for surprise that it has run to six editions. As might be expected from the distinguished author, the chapters on fractures and deformities have been brought well up to date and illustrated. Perhaps it is too much to expect that in a single small volume everything in surgery should be thoroughly modernised, but we think in the next edition several not very rare conditions might deserve a word, *e.g.* idiopathic renal hæmaturia, B. coli infections of the prostate, sacroiliac strain, local tetanus, mobile cæcum mimicking appendicitis, etc. It is not mentioned that a valuable sign of gastric carcinoma is a filling defect in the X-rays, and the value of X-ray treatment for lymphadenoma might be mentioned. Some statements would scarcely receive wide acceptance to-day; for instance, it is stated that the normal stomach empties in two hours, and that $MgSO_4$ is " of great value " in the treatment of tetanus. In the treatment of trigeminal neuralgia removal of the ganglion is spoken of as the method of choice in all severe cases, and division of the sensory root, which many would prefer, is said to be done through the *posterior* cranial fossa, which is not the best modern method in our judgment. However, surgery is not a finished

science, and no one will ever write a book that will command universal acceptance for every sentence. The book is beautifully turned out, as befits the house that prints it, which is a credit to our town.

Tumours Complicating Pregnancy, Labour, and the Puerperium. By HERBERT R. SPENCER, M.D., B.S. Pp. 78. London: Harrison & Sons. Price 5s. net.—This book is a reprint of the author's Lettsomian lectures; it is unnecessary to say that the general presentation of the subject and the accuracy of the clinical observations recorded in the subject matter of the lectures are all that might be expected from the author. The lectures form a most valuable contribution to the literature on the subject: the clinical material is ample, its analysis masterly, and the conclusions drawn therefrom based on sound logical reasoning. Dealing with the cases in detail, the author shows that as regards fibroids a quite definite proportion of cases in which these tumours complicate pregnancy require operative treatment, as operative emergencies necessitated by degenerative processes occurring in the tumour, and that of these, unless operation is unduly delayed, a large proportion can be dealt with by myomectomy without interrupting the pregnancy. The author's findings are in accord with the experience of most of those who have found it necessary to deal with cases of the kind. Of the cases dealt with by Cæsarean section it would perhaps have been better to exclude, or to place in a separate table, those in which the operation was necessitated by contracted pelvis and not primarily by the fibroid. This, however, does not prevent sound deductions as to the necessary indications for operations being drawn from the cases quoted. As regards ovarian tumours, the presentation of the cases is most complete and the deductions drawn are very sound. The treatment is worth summarising as follows: 1. During the first half of pregnancy ovarian tumours (with a few exceptions) should be removed wherever their situation and whatever their size. 2. During the second half of pregnancy: (*a*) All large tumours and all others showing signs of pathological changes should be removed; (*b*) small *abdominal* tumours not producing symptoms may be left if under constant observation. 3. During labour immediate ovariotomy for *all large* tumours. Small tumours at end of first stage or immediately after delivery. Cæsarean section is necessary in rare cases of adherent or solid tumours in pelvis, but no such measures as induction of labour, forceps, version or tapping to relieve dystocia should be considered.

Lawson Tait: His Life and Work. By W. J. STEWART MCKAY, M.B. Pp. xii., 579, London: Baillière, Tindall & Cox. 1922. Price 25s. net.—This work gives a most interesting

account of the life and work of one who was, by common consent, regarded during his life as one of the pioneers of Surgery. It will be of interest to those who knew him personally, but probably even more interesting to those who knew of him only as a contemporary worker. It is a record of a man possessed of an enormous capacity for overcoming difficulties, of boundless energy and unflagging industry; who was possessed of exceptional clinical acumen and manual dexterity, which made him an outstanding figure in a generation which contained many giants. The soundness of his work is attested by the fact that most of his methods have been preserved by his successors, thus proving that they were based on sound surgical reasoning. The cases cited in connection with controversies which arose over various procedures which he advocated make particularly good reading. Space does not allow a detailed account of these, but it must be noted with regard to Tait's operation and methods in ectopic gestation that although he discarded, and rightly, the vaginal route in dealing with this particular complication, his assistant and successor, Professor Taylor of Birmingham, made use of it not infrequently in our experience, as a method of clearing up the diagnosis in doubtful cases, when for any reason it did not seem advisable to perform an exploratory laparotomy for that purpose. A certain degree of intolerance, perhaps most marked in his attitude towards Lister and his methods, is to be noticed, as also a certain capacity for special pleading which at times approaches the boundary of strict scientific truth. The latter is demonstrated in his controversial speeches and writing. In spite of this, the author presents the picture of a man of enormous capacity, both intellectual and physical, of great originality and strong personality. There is little doubt that a certain harshness in dealing with opponents, a degree of intolerance of the opinions of others, and his special pleading were due to his early difficulties and to the opposition to which, he, like all other pioneers, was exposed. The methods of some of his opponents, as described by the author, were the reverse of creditable, and, as we know, jealousy was responsible for a good deal. The author depicts Tait in his private life as he was—somewhat of a *viveur*, a sportsman, a genial companion, a firm friend, a connoisseur of art and literature and, in fact, a man *teres atque rotundus*.

Venereal Disease in the American Expeditionary Forces. By GEORGE WALKER, M.D., late Colonel, Medical Corps, U.S.A. Pp. xxiii., 237. Baltimore; Medical Standard Book Co. 1922. —This book shows the methods which really proved effective in the control of Venereal Disease in France. The author

states, " After a close study of conditions in France, it became evident that in order to limit very materally venereal infection, our chief reliance would have to be placed on prophylaxis." The most stringent measures were adopted to prevent the incidence of the disease. General Pershing commenced the campaign by penalising every patient. This was soon followed by an order by which failure to apply prophylaxis was also punished. Owing to the great loss of time incurred by the British and French Armies, because of their system of treating Venereal Disease in base hospitals, it was decided to retain venereal patients with their own units and treat them at the regimental infirmary, except when complications existed in which case the men were sent to special hospitals. When Divisions went into line the Venereal Disease victims were detained in the area of the Divisional operations. It was found that 71 per cent. of all American soldiers in France had sex relations during the stay in that country. Before orders were enforced for compulsory prophylaxis, venereal infection amongst the first troops in France was found to be 240 per thousand per year among the whites, and 625 per thousand per year amongst the coloured. Compulsory prophylaxis soon reduced the rate to almost zero per thousand among the whites, and 20 per thousand among the coloured. A record of 242,000 exposures showed only 1.3 per cent of failure. All leave areas, Red Cross huts, and even leave trains provided stations with skilled attendants and medical officers in charge. Comparative incidence of Venereal Disease showed Gonorrhœa, 52 per cent ; Chancroid, 40 per cent ; Syphilis, 8 per cent. An interesting fact was that 42 per cent. of all sores proved by dark field illumination to be syphilitic. The book is pleasantly written, disclosing faithful and painstaking compilation from a multitude of sources, and will well repay study.

Editorial Notes.

Professor E. Fawcett, F.R.S.

THE election of Professor Fawcett to the Fellowship of the Royal Society has given great satisfaction to all his colleagues and to many generations of Bristol Medical Students.

Professor Fawcett came to Bristol in 1893 to fill the newly founded Chair of Anatomy in University College. In 1905 he succeeded Dr. Markham Skerritt as Dean of the Faculty of Medicine. He has held both these offices with notable distinction and much advantage to the University. His researches in Anatomy, more particularly those dealing with the comparative morphology of the chondro-cranium won world-wide recognition, so that it was no surprise to Bristol that he should be elected F.R.S. As a teacher of Anatomy we have long since realised that he stood in the front rank. His prowess in the cricket-field, his knowledge of ecclesiastical architecture, and his wide acquaintance with archæology and anthropology bear witness to the universality of his interests.

We offer Professor Fawcett our heartiest congratulations that the Royal Society should have crowned his labours with such a well-earned honour.

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Resignation of Miss A. B. Baillie, R.R.C.

IT is with great regret that we have to record the resignation of Miss Baillie from the Matronship of the Royal Infirmary.

Miss Baillie received her nursing training under Miss Luckës at the London Hospital, where she became Sister of the Surgical and Accident Wards, and later Matron's Office Assistant. In 1896 she was appointed

Matron of the Hospital of St. Cross at Rugby. In 1898 she succeeded Miss Smith as Matron of the Bristol Royal Infirmary. Her work there is too well known to need detailing. Under her guidance the nursing department has made marvellous progress. More than twenty of her nurses at present occupy matron's posts.

As soon as she assumed office she materially increased the number and the efficiency of the nursing staff. The New Nurses' Home and its magnificent garden owe their existence to her energy. She started a massage school for nurses at the Infirmary in 1904, and a preliminary training school for nurses in 1908, the first to be opened in the provinces. One great innovation which Miss Baillie was the first Matron in the country to practise was that of giving each nurse a whole day off duty every week. The present successful midwifery school for nurses is another proof of her organising ability—and the new lying-in wards which were opened after the war were in large part due to her endeavours. On the formation of the Territorial Force Nursing Service, Miss Baillie was made a Principal Matron. Her work in this capacity during the war was beyond praise; and when she received the order of the Royal Red Cross (first class) in 1915, it was universally felt that no one had more richly deserved the honour. She had not only been responsible for the staffing of the 2nd Southern General Hospital with nurses, but had also contributed largely to the organisation of many subsidiary Red Cross Hospitals in the Southern Command and had arranged for the supply of nurses to these hospitals.

For the past three years Miss Baillie has been a member of the Army Nursing Council, and she is also on the Council of the College of Nurses.

In 1922 the Committee of the Bristol Royal Infirmary in recognition of the great part played by her in the develop-

ment of the maternity department named one of the wards the " A. B. Baillie " Ward.

Miss Baillie is now leaving the Infirmary to become the first Matron of the St. Monica's Home for incurables, founded by the late Mr. H. H. Wills.

She takes with her to her new work the good wishes of all who have worked with her, and a feeling of confidence that her unabated energy and organising capacity will ensure the success of St. Monica's Home.

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Colston Research Society.

THE Annual Dinner of the Colston Research Society was held at the Victoria Rooms, Clifton, on Friday, June 1st, under the presidency of Mr. Claude Fry, and was well attended. The Toast List was a short one, the principal speeches being those of Sir W. M. Petrie and Sir Richard Gregory, the two guests, who replied to the Toast of their health proposed by the Vice-Chancellor. The Presidential Collection amounted to £669 8s. 6d., and it was satisfactory to learn that the Colston Research Fellowship Scheme initiated last year has been so successful that five out of the six firms then donating Fellowships have renewed them for a further period, and two other firms have taken advantage of the Scheme, making seven Fellowships in all. The Society is making headway and getting increased support from the Commercial Community, between whom and the University it is helping to promote a closer liaison.

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The British Journal of Surgery.

THE *British Journal of Surgery* enters with the July number just published upon the eleventh year of issue. The long continuance of the Great War sadly handicapped its production by doubling, and at one time

actually trebling, its cost. The wonderful way in which members of the Medical Profession generally continued to support their new Journal during those trying years will always remain a happy memory with the proprietors. It is therefore with pride as well as pleasure that they find themselves able, with the commencement of the present volume, to return to practically pre-war conditions. The type is improved, the pages are increased to 200 per number, and no opportunity is being missed to enhance still further the value of the contents and the way in which it is presented. This publication not only represents the highest attainments of British Surgery, but also exhibits the best that is obtainable in artistic medical journalism.

Meetings of Societies.

THE Meeting of the Society, held on May 16th in the Lecture Theatre of the Bristol Museum and Art Gallery, was an event of exceptional interest ; Mr. T. Howard Somervell, F.R.C.S., one of the members of the recent expedition to Mount Everest, gave an address on the subject of " The Problems of Living at High Altitudes." There were present : the President, Dr. J. A. Nixon, C.M.G., in the Chair ; the Pro-Chancellor of the University, Mr. G. A. Wills ; the Sheriff of Bristol, Mr. Horace Walker, D.L., J.P.; the Master of the Society of Merchant Venturers, Mr. Gerald Beloe ; and about 300 members and their guests. The address was illustrated by lantern slides from the author's camera and by parts of the official film, showing the actual ascent of the mountain. The country through which the expedition approached the mountain was shown, with interesting accounts of the Tibetan manners and customs. The lecturer then described the actual ascents made by three parties, of which he

took part in two. The film enabled one to imagine the vast physical obstacles that were encountered.

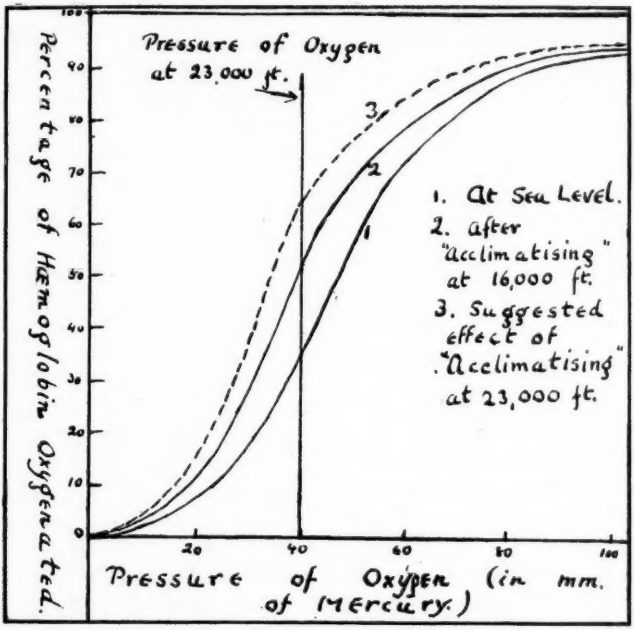
The actual attempts on the mountain were made from an advanced base camp at a height of 23,000 ft. The expeditions from this point calculated to be away for four days at a time. The first attempt, made without oxygen, reached an altitude of 27,000 ft.; the second, with oxygen, 27,250 ft.; the third was, as all remember, overwhelmed in an avalanche, with seven deaths. This disaster and the bad weather which caused it brought the expedition to a close.

The problems of scientific interest to which Mr. Somervell alluded were many. The expedition was not primarily engaged upon physiological research, nor could any apparatus beyond the absolutely essential be transported so far. The most interesting points are those relating to oxygen supply.

Although it had previously been thought impossible, it was clear that "acclimatisation" took place even at so great a height as 23,000 ft. Three factors are involved in the adjustment to low oxygen tension: (1) Increased rate of heart beat and of respiration. The lecturer observed that at 27,000 ft. his pulse was 180, respirations 55 per minute. For this to continue for several days it is clear that only a young and healthy heart is adequate; a mitral insufficiency developed in some cases but passes off later. (2) Concentration of red corpuscles in the blood to approximately double the normal; in addition to an absolute increase in number, there is a diminution in the volume of serum. (3) Barcroft has shown that hæmoglobin increases its power of taking up oxygen when the oxygen tension is for several days reduced. Mr. Somervell suggests that the process which occurs in rising to 16,000 ft., at which the published experiments were conducted, continues; and points out that if so nearly twice the "sea level" oxygenation will be found. In the sketch diagram (not to scale) the dotted line represents the suggested curve acclimatised at 23,000 ft.; a percentage of 65 oxygenation instead of the 35 per cent. at "sea level adjustment" is shown on next page. The combined effect of these processes was very noticeable after several days' living and climbing at 23,000 ft.

During the early part of the ascent to the advanced base

camp mountain sickness was noticed by everyone at 17,000 ft., but it soon passed off. At the higher camp appetites failed, but in many cases they returned as acclimatisation occurred. Administration of oxygen was also found to restore the appetite. Anorexia appeared to be a definite effect of oxygen starvation. This symptom proved serious in one or two of the older members of the party; they did not "acclimatise," and partial starvation increased their troubles at the higher altitudes.


Percentage of Hæmoglobin Oxygenated.
Pressure of Oxygen at 23,000 ft.
1. At Sea Level.
2. After "Acclimatising" at 16,000 ft.
3. Suggested effect of "Acclimatising" at 23,000 ft.
Pressure of Oxygen (in mm. of Mercury.)

In the second attempt oxygen in cylinders sufficient for eight hours was carried; the apparatus, however, weighed thirty-four pounds, and this, in Mr. Somervell's opinion, more than counterbalanced its advantages. The fact that eight Nepali bearers were required to carry the apparatus to the advanced camp (from the advanced base) was a serious factor. Mr. Somervell felt convinced that better results will be obtained

by men who acclimatise at high altitudes and then ascend without the apparatus, as by these tactics a larger number of attempts can be made in one season.

Cold was severe; twelve thicknesses of clothing were worn, and more would have been better; only one member suffered severely from frost bite. The cold itself recorded was never below −20° F, but it was rendered more severe in effect by the high wind. Atmospheric conditions, however, are of the utmost importance. Snow or a high wind render an ascent out of the question, and these are apt to prevail on two days out of three. The monsoon makes the snow unsafe for climbing; a recent fall of soft snow resulted in the fatal avalanche which terminated the third attempt. Thirst was a severe enemy; water could only be obtained by melting the snow, and therefore depended on fuel; the allowance of drinking water was very limited during the ascent. One member of the first party became seriously ill from thirst and could not continue the climb. The party were thirty-six hours without water, and were unable, in consequence, to eat.

The mental effects of oxygen-want were interesting. All the climbers suffered from bad temper. A certain irresponsibility was observed. Mr. Somervell did not suffer any disappointment at having to abandon the first climb. The second party took a camera up and forgot to use it.

The lecturer concluded by expressing a hope that another British expedition might be equipped to go out in 1924. This was solely a question of funds; £14,000 was needed to make another attempt. If the attempt were delayed possibly some other nation would "get there first."

Dr. P. Watson-Williams moved a vote of thanks to the lecturer for his admirable account, and expressed the pleasure it and the unique films had given. He was convinced that Bristol would lead the way in equipping next year's expedition. In this conviction Mr. Walker, the Sheriff, and Mr. Beloe, Master of the Merchant Venturers, joined. Mr. T. Carwardine seconded the vote, which was carried by acclamation.

Local Medical Notes.

UNIVERSITY OF BRISTOL.—Students of the University have recently passed the following examinations :—

F.R.C.S. ENG.—W. Salisbury.

M.B., CH.B. BRISTOL.—*Second Examination :* J. F. O. Bodman, A. H. Bright, A. J. M. Grimston, F. W. T. Hughes. *Final Examination* (*2nd Class Honours*) *:* F. H. Bodman, Constance L. Griffiths. *Pass :* D. Staley, I. Williams, *Part I.* (*including Forensic Medicine*) *:* E. R. Clutterbuck, E. B. Eedle, J. A. James, F. G. Jenkins, F. Langford, G. S. Mundy, A. S. Prowse. *Part I. only :* R. H. Dummett, K. F. Platt. *Forensic Medicine only :* Helen M. Dixon.

CONJOINT EXAMINING BOARD.—*Medicine :* W. Gornall, A. E. Sherwell, G. Murray-Shirreff, E. G. Bradbeer, *Carrie H. Osmond, Hilda R. Dutton. *Surgery :* Carrie H. Osmond, J. R. Nicholson-Lailer, H. M. Golding, *W. A. Gornall, C. Powell. *Midwifery :* Edna V. Butler, C. F. Wilson, J. R. Nicholson-Lailey, R. C. Hatcher, E. G. Bradbeer, H. R. Dutton, W. A. Gornall, J. L. Griffin, A. G. Heron, Doris E. Joscelyne, E. F. King, A. E. Sherwell.

L.D.S., R.C.S. ENG.—D. J. Andrews.

L.D.S. BRISTOL.—*Second Examination :* W. B. Bowrey, A. W. Cawsey, C. S. Cossham, R. G. Downes, D. Griffiths, C. H. Hill, H. F. Lane, S. Phillips, B. F. Robinson, Agnes M. Thoseby, G. C. Brooks. *Anatomy only :* C. P. Winstone. *Third Examination :* G. C. Friend. *Final Examination :* V. E. N. Allen, H. N. V. Barnes, S. H. Bedford, A. S. C. Boulter, M. P. Browning, A. H. Butcher, R. G. Butterworth, H. P. Evans, G. Holt, A. R. Hutchings, C. Lewis, F. C. G. Lewis, J. C. W. Lewis, R. C. Price, J. F. Rigg, J. S. Roberts, W. H. Simpkiss, C. E. Smith, E. K. Tratman, Kathleen M. Watson, F. C. Winter.

L.M.S.S.A.—M. M. Lopez.

* Qualified.